COMPARISON OF RECENT PISA MODEL WITH REVISED GENEVA SCORE AND WELL'S SCORE IN PREDICTING THE PROBABILITY OF PULMONARY EMBOLISM IN INDIAN CONTEXT

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CERTIFICATE

This is to certify that the dissertation entitled **COMPARISON OF RECENT PISA MODEL WITH REVISED GENEVA SCORE AND WELL'S SCORE IN PREDICTING THE PROBABILITY OF PULMONARY EMBOLISM IN INDIAN CONTEXT"** is the bonafide original work of **DR.M.A.ARUMUGAM** in partial fulfillment of the requirements for **D.M.Branch-II (CARDIOLOGY)** examination of **THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY** to be held in August 2011. The period of post-graduate study and training was from July 2008 to July 2011.

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DECLARATION

I Dr.M.A.ARUMUGAM, solemnly declare that this dissertation entitled, **COMPARISON OF RECENT PISA MODEL WITH REVISED GENEVA SCORE AND WELL'S SCORE IN PREDICTING THE PROBABILITY OF PULMONARY EMBOLISM IN INDIAN CONTEXT** is a bonafide work done by me at the department of Cardiology, Madras Medical College and Rajiv Gandhi Government General Hospital during the period 2008 – 2011 under the guidance and supervision of the Professor and Head of the department of Cardiology of Madras Medical College and Government General Hospital, Professor Geetha Subramanian, M.D.D.M. This dissertation is submitted to The Tamilnadu Dr.M.G.R Medical University, towards partial fulfillment of requirement for the award of D.M. Degree (Branch-II) in Cardiology.

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CONTENTS

INTRODUCTION

Acute pulmonary thromboembolism afflict lakhs of people throught the world and is the third most common problem after coronary artery disease and cerebrovascular accident. The case fatality rate is 15 percent and it exceeds the mortality rate of acute myocardial infarction

The high mortality rate of pulmonary embolism is failure to diagnose or suspecting in an appropriate patient

In autopsy studies when the pathologist judged PE contributed to the death, the diagnosis was unsuspected ante-mortem in over one- half cases

Awareness of PE for clinicians is important at all levels of care so that early diagnosis and proper timely referral are made

In 1856 Rudolf Virchow postulated that a triad of factors predisposed to thrombosis

1) Local trauma to the vessel
2) Hypercoagulability
3) Stasis

One of the above factors or combination of the factors lead to PE

In the era of lot of air travel, people are more prone for PE[1,2]

Nowadays lot of old age people are undergoing surgery and they are kept immobile making them prone for PE.

Obesity has become common as people are using vehicles for even short distance.For each 40% increase in weight there is two fold increase in incidence of PE.[3]

Incidence of PE increases exponentially with age and is more frequent in adults than in children.[4]

Incidence of PE is more common in smokers.

Malignancy incidence is increasing and treatment with chemotherapy heightens the risk of DVT and PE.[5]

Stroke and congestive heart failure are predisposing factors.

Inherited hypercoagulable factors remains silent until an acquired stress occurs.

Immobilization irrespective of the cause is the most frequent predisposing factor.

Deep Venuos Thrombosis is the origin of PE in 80% of cases.A difference of circumference of the calves of 1 cm or more, measured 10 cm below the tibial tuberosity is abnormal. Valve pockets are frequent site of origin of thrombi.These venous thrombi detach from their sites of formation they flow toward the vena cava,they go to right atrium, right ventricle and enter pulmonary artery.DVT is detected only in 30% of the cases after they embolize to pulmonary circulation.

The extent of pulmonary obstruction will determine the severity, clinical features and the prognosis.

Small to moderate PE patients are clinically stable.

Moderate to large (sub massive) PE patients have one third or more of the vasculature obstruction.

Massive pulmonary embolism patients have thrombosis affecting atleast half of pulmonary arterial vasculature.

As obstruction increases pulmonary hypertension is caused by chemicals such as serotonin, reflex vasoconstriction and hypoxia.

The overloaded right ventricle release biomarkers such as brain natriuretic pepetide and troponin.[6]

As the right ventricle dilates the intervenricular septum shifts to left leading to hypotension.

Increased wall tension of RV reduces right coronary flow and causes ischemia.[7]

PE at the bifurcation leads to collapse of the patient. More commonly embolus lodges at one of the branches of pulmonary artery.

In a French study when PE was diagnosed appropriate citeria was used in 92% of patients but when PE excluded inappropriate criteria were used in 57% of the cases.[8]

Two factors predisposed to error

1 Lack of algorithm

2 Not doing additional tests in elevated D-dimer cases

Another problem is delayed presentation.[9]

PE is a great masquerader of diseases.

Symptoms like dyspnoea are often thought of as symptom of other diseases.

Signs are that of right ventricular hypertension that are obvious in some of the cases.

Investigations like ecg echocardiogram ,D-dimer [10] Ventilation-Perfusion scan CT scan are helpful.

So the diagnosis of PE requires constellation of predisposing factors, symptoms, signs and investigations and high degree of suspiscion.

PE when it is massive or sometimes submassive is an emergency where we have to asses the probability of PE quickly to proceed further.

PROBABILITY OF PE

To assess the probability of PE in a patient there are two models WELLS(Canada) and revised GENEVA that are currently followed .

WELLS model takes in to account-mostly positive variables

- DVT symptoms or signs,
- No alternate diagnosis,
- Heart rate,
- History of immobilization or surgey within 4 weeks,

- Prior DVT or PE,
- Haemoptysis,
- Cancer treated within 6 month or metastatic

REVISED GENEVA MODEL takes into account-positive variables

- Age
- Previous DVT or PE
- Surgery or fracture in 1 month
- Active malignancy
- Unilateral limb pain
- Haemoptysis
- Heart rate
- Pain on lower limb deep vein palpation and unilateral oedema

In PISA CITY of ITALY, Miniati et al introduced PISA MODEL for the prediction of PE[11].

PISA MODEL contains 10 positive variables and 6 negative variables and takes into account ECG findings

- 10 positive variables:
  - Older age
  - Male sex
  - Prolonged immobilisation
  - History of DVT
  - Sudden onset dyspnea

    - Chest pain
    - Syncope
    - Hemoptysis
    - Unilateral leg swelling
    - Ecg signs of acute cor pulmonale
- 6 negative variables:
    - Prior cardiovascular disease
    - Prior respiratory disease
    - Orthopnea
    - High fever
    - Wheeze
    - Crackles

PISA MODEL FORMATION-PROCESS

This model was developed from Pisa city Italy by Miniati et al from the centre of excellence for pulmonary embolism[11]

Sample prevalence was done for all the variables collected in the 1,100 patients, separately for patients with and those without pulmonary embolism. Age was the only continuous variable, and it was grouped into four classes based on the quartiles of its observed distribution (15–56, 57–67, 68–74, and 75–94 yr).

The univariate relationship between patients' baseline characteristics and the diagnosis of pulmonary embolism was assessed by Fisher's exact test or by Mann-Whitney nonparametric test. Two-tailed P values less than 0.05 were considered statistically significant throughout.

Logistic regression model for the probability of having pulmonary embolism was done.

Initially, all the baseline variables were included in the model. Then, they were removed one by one, if not statistically significant. If the removal caused large changes (>10%) in the coefficients of any of the remaining variables, the removed variable was reintroduced into the model. In the model-building process, age and sex were considered known relevant predictors and were kept in the model regardless of their statistical significance.

In the final model, however, all the variables included were statistically significant. The area under the receiver operating characteristic (ROC) curve of the final model was reported, together with its 95% confidence interval (CI). All the analysis was performed on Stata (STATA 10; StataCorp, College Station, TX) and R software

INTERNAL VALIDATION OF THE MODEL

To estimate the predictive accuracy of model, when applied to a new set of patients, bootstrap resampling techniques was used. The area under the ROC curve from 1,000 bootstrap samples of size 1,100 that were randomly selected with replacement from the original 1,100-patient sample.

EXTERNAL VALIDATION OF THE MODEL

The predictive model, derived from the original 1,100-patient sample, was validated in an independent sample of 454 patients with suspected pulmonary embolism who were evaluated between January 1, 2003, and December 31, 2005. Fifty-four (12%) of them were excluded because of inability to obtain an informed consent (n = 28), or documented contraindications to pulmonary angiography (n = 26). The remaining 400 patients were managed according to the diagnostic protocol described above. The clinical probability of pulmonary embolism was estimated at bedside by one of seven residents in respiratory medicine by using the proposed software on palm computers. Clinical probability was assessed before any further objective testing.

DERIVATION SAMPLE

The 1,100 patients in the derivation sample had a median age of 68 years (interquartile range [IQR], 57–75 yr); 45% of them were male, and 81% were hospitalized at the time of study entry. On the basis of angiography and autopsy findings, the prevalence of pulmonary embolism was calculated

PREDICTIVE MODEL

Sixteen variables were incorporated into a multivariate logistic regression model, of which 10 were positively and 6 were negatively associated with pulmonary embolism.

Variables associated with an increased likelihood of pulmonary embolism were as follows: older age, male sex, prolonged immobilization, history of deep vein thrombosis, sudden-onset dyspnea, chest pain, fainting (or syncope), hemoptysis, and electrocardiographic signs of acute cor pulmonale.

Variables associated with a decreased likelihood of pulmonary embolism included prior cardiovascular or pulmonary disease, orthopnea, high fever, wheezes, or crackles on chest auscultation. The area under the ROC curve was 0.90 (95% CI, 0.88–0.91)[12].

The probability of pulmonary embolism can be calculated after adding all the applicable regression coefficients to the constant.

Among the 440 patients with pulmonary embolism, there was a highly significant, positive relation between the clinical probability predicted by the model

INTERNAL VALIDATION

The predictive model derived from the original 1,100-patient sample appeared to be accurate and parsimonious. The overall accuracy of the model, as measured by the ROC area, was validated based on 1,000 bootstrap samples. The area under the ROC curve on a sample of new independent patients was estimated to be 0.88.

EXTERNAL VALIDATION

The 400 patients in the validation sample had a median age of 70 years (IQR, 59–76 yr); 42% were male, and 71% were inpatients at the time of study entry.

Pulmonary embolism was diagnosed by angiography in 165 (41%) of 400 patients. The median extent of pulmonary vascular obstruction at baseline was 40% (IQR, 27–56%). Of the 235 patients without pulmonary embolism, 83 had normal perfusion scans. None of them presented with symptomatic episodes of venous thromboembolism over a 6-month follow-up.

The proportion of patients in each of probability categories and the relative prevalence of pulmonary embolism are reported in or the whole sample, and separately for inpatients and outpatients. In the validation sample, the area under the ROC curve was 0.88 (95% CI, 0.84–0.91), which was consistent with the estimate from the internal validation.

The prevalence of pulmonary embolism in outpatients (46%) was slightly but not significantly higher than in inpatients (39%, P value = 0.18 by Fisher's test). There was no significant difference between inpatients and

outpatients regarding the prevalence of pulmonary embolism in each of the probability categories.

In the 165 patients with pulmonary embolism at inclusion, there was a highly significant, positive relation between the clinical probability predicted by the model and the severity of pulmonary embolism on the lung scan (P value < 0.001 by Kruskal-Wallis nonparametric test).

Pisa model is entirely based on the evaluation of relevant clinical symptoms and signs, and the interpretation of the electrocardiogram. Therefore, it is applicable in any clinical context

In terms of predictive accuracy, model outperformed those reported by others The area under the ROC curve was 0.90 in the derivation sample, and 0.88 in the validation sample.

Among the patients with pulmonary embolism, there was a strong relation between the clinical probability predicted by the model

AIM OF THE STUDY

- To compare Pisa Model with Wells Score and Revised Geneva Score in predicting the probability of pulmonary embolism

- To validate Pisa Model in predicting the probability of pulmonary embolism in Indian context

REVIEW OF LITERATURE

Approximately 100,000 patients in the United States die each year directly as a consequence of acute pulmonary embolism (PE), with another 100,000 deaths occurring in patients with concomitant disease in whom PE contributes significantly to their demise[13,14]. Three-month mortality in unselected patients with acute PE is as high as 15 percent[15].

Although a number of patients die of comorbidities that predisposed them to the thromboembolic event, a substantial number of patients die from PE within an hour of presentation, before the diagnosis can be confirmed and therapy initiated, or because the diagnosis was overlooked.

Autopsy studies have repeatedly documented the high frequency with which PE has gone unsuspected and undetected. Despite advances in diagnostic imaging tests and therapeutic interventions, PE remains underdiagnosed and prophylaxis continues to be dramatically underused.

Anticoagulation with heparin as a "bridge" to warfarin is still considered the standard treatment for PE. The spectrum of anticoagulant drugs has been expanded recently. Low-molecular-weight heparins (LMWHs) have been shown to be effective and safe for both treatment and for prevention of VTE, particularly in hospitalized medical patients.

Fondaparinux, a new pentasaccharide, is very effective in a fixed low dose in preventing venous thromboembolism (VTE) after orthopedic and abdominal surgery, and has been demonstrated in clinical trials to be as

effective as LMWH and unfractionated heparin for the initial treatment of patients with deep venous thrombosis and pulmonary embolism.

RISK FACTORS AND PATHOGENESIS OF VENOUS THROMBOEMBOLISM

In 1856, Virchow proposed his triad of factors leading to intravascular coagulation, including stasis, vessel wall injury, and hypercoagulability. Risk factors for deep venous thrombosis (DVT) are based on these processes

The overwhelming majority of emboli originate from the deep veins of the lower extremities, although any venous bed can be involved. in wall, most originate in valve pockets.

The veins of the calf are the most common site of origin, with subsequent extension of the clot prior to embolization. Eventually, the thrombus may expand to fill the vessel entirely, with both retrograde and proximal extension. If embolization does not occur, the thrombosis can partially or completely resolve via three mechanisms: recanalization, organization, and lysis.

RISK FACTORS FOR VENOUS THROMBOEMBOLISM

Acquired factors

- Age older than 40
- Prior history of venous thromboembolism
- Prior major surgical procedure
- Trauma
- Hip fracture
- Immobilization/paralysis

- Venous stasis
- Varicose veins
- Congestive heart failure
- Myocardial infarction
- Obesity
- Pregnancy/postpartum period
- Oral contraceptive therapy
- Cerebrovascular accident
- Malignancy
- Severe thrombocythemia
- Paroxysmal nocturnal hemoglobinuria
- Antiphospholipid antibody syndrome (including lupus anticoagulant)

Inherited factors

- Antithrombin III deficiency
- Factor V Leiden (activated protein C resistance)
- Prothrombin gene (G20210A) defect
- Protein C deficiency
- Protein S deficiency
- Dysfibrinogenemia
- Disorders of plasminogen
- Hyperhomocysteinemia

Acquired Risk Factors

Long automobile or airplane trips appear to be risk factors for VTE, and correlates with the flight distance. The risk of PE significantly increases with a flight distance >3107 miles (5000 km) or a duration >8 hours.

Obesity merits further investigation, because recent studies implicate obesity as a risk factor for VTE, body mass index 29 kg/m2 was an independent risk factor. The Framingham Study has confirmed that obesity is a risk factor for PE, particularly in women[16].

In addition to increased venous stasis, obesity may also increase the risk for VTE as a consequence of elevated plasma levels of certain clotting factor such as fibrinogen, factor VII, and plasminogen activator inhibitor-1, and as a result of platelet activation caused by enhanced lipid peroxidation.

An abundance of literature documents that the risk of venous thromboembolism increases with age, with a relative risk for those 70 years of age approximately 25-fold greater than the risk for those 20 to 29 years of age..

Surgical patients with a previous history of VTE who do not receive prophylaxis develop postoperative DVT in more than 50 percent of cases. Surgery itself significantly enhances the risk. Patients who are undergoing general surgery without additional risk factors develop DVT in nearly 20 percent of cases if neither pharmacologic nor mechanical prophylaxis is applied. Patients who are undergoing lower-extremity orthopedic procedures such as total hip or total knee replacement develop DVT in more than 50 percent of cases.

Trauma, particularly of the lower extremities and pelvis, heightens the risk of DVT. PE has been identified at autopsy in as many as 60 percent of patients with lower-extremity fractures, and mortality has been attributed to

PE in as many as 50 percent of patients dying after hip fracture. Upper-extremity DVT has become more important because of an increasing use of pacemakers, implantable defibrillators, and long-term, indwelling, central venous catheters. Symptomatic PE can originate from upper-extremity thrombi, although this appears much less common than embolization from lower-extremity DVT.

Upper-extremity DVT poses the risk of superior vena cava syndrome and loss of vascular access. Effort-related, upper-extremity axillosubclavian thrombosis ***(Paget-Schroetter syndrome)***[17] may occur spontaneously or be associated with an underlying thrombophilic tendency, and may result in significant, long-term functional impairment.

Epidemiologic analyses, as well as autopsy data, suggest that patients with cardiac disease are predisposed to VTE Although myocardial infarction without anticoagulation is associated with a significant incidence of DVT, more recent therapeutic strategies for acute coronary syndromes have had a beneficial impact. Large, placebo-controlled acute myocardial infarction trials indicate that the use of thrombolytic therapy reduces the incidence of VTE.

Cancer clearly augments the risk of VTE

Following the administration of various chemotherapeutic agents, changes in the levels of coagulation factors, suppression of anticoagulant and fibrinolytic activity, and direct endothelial damage have been documented clinically and experimentally

Hormonal therapy, particularly tamoxifen in breast cancer adjuvant therapy, is also associated with an increased risk of thromboembolism, particularly when combined with chemotherapy.

Neutropenia and sepsis, which often accompany chemotherapeutic regimens, often necessitate hospitalization and bedrest, which contributes further to the risk of VTE

DVT appears to be more common in the third trimester and postpartum than prior to delivery, the risk is considerable throughout pregnancy.

Cesarean section further augments the risk.

Oral contraceptives are associated with an increased relative risk of venous thromboembolism, although the absolute risk (approximately 1 to 3 cases per 10,000 woman-years) remains small.

Oral contraceptive use should be avoided bywomen with protein C, protein S, and antithrombin III deficiency, as well as those who are homozygous carriers of the factor V Leiden mutation.

PATHOPHYSIOLOGY OF ACUTE PULMONARY EMBOLISM

GAS-EXCHANGE ABNORMALITIES

Hypoxemia and hypocarbia are associated with acute embolism

HEMODYNAMIC ALTERATIONS

The hemodynamic effects of embolism are related to three factors: the degree of reduction of the cross-sectional area of the pulmonary vascular bed,

the preexisting status of the cardiopulmonary system, and the physiologic consequences of both hypoxic and neurohumorally mediated vasoconstriction. Obstruction of the pulmonary vascular bed by embolism acutely increases the workload on the right ventricle, a chamber ill-equipped to deal with high-pressure load. In patients without preexisting cardiopulmonary disease, obstruction of less than 20 percent of the pulmonary vascular bed results in a number of compensatory events that minimize adverse hemodynamic consequences. Recruitment and distension of pulmonary vessels occur, resulting in a normal or near-normal pulmonary artery pressure and pulmonary vascular resistance; cardiac output is maintained by increases in the right ventricular stroke volume and increases in the heart rate. As the degree of pulmonary vascular obstruction exceeds 30 to 40 percent, increases in pulmonary artery pressure and modest increases in right atrial pressure occur. The Frank-Starling mechanism maintains right ventricular stroke work and cardiac output.

When the degree of pulmonary artery obstruction exceeds 50 to 60 percent, compensatory mechanisms are overcome, cardiac output begins to fall, and right atrial pressure increases dramatically. With acute obstruction beyond this amount, the right heart dilates, right ventricular wall tension increases, right ventricular ischemia may develop, the cardiac output falls, and systemic hypotension develops. In patients without prior cardiopulmonary disease, the maximal mean pulmonary artery pressure capable of being generated by the right ventricle appears to be 40 mmHg. The correlation between the extent of pulmonary vascular obstruction and the pulmonary vascular resistance appears to be hyperbolic, reflecting at its lower end the

expansible nature of the pulmonary vascular bed, and at its upper end, the precipitous decline in cardiac output that may occur as the right ventricle fails.[18,19] The hemodynamic response to acute pulmonary embolism in patients with preexisting cardiopulmonary disease may be considerably different. Patients with prior cardiopulmonary disease demonstrate degrees of pulmonary hypertension that are disproportionate to the degree of pulmonary vascular obstruction. As a result, severe pulmonary hypertension may develop in response to a relatively small reduction in pulmonary artery cross-sectional area. Thus, evidence of right ventricular hypertrophy (rather than right ventricular dilatation) associated with a mean pulmonary artery pressure in excess of 40 mmHg should suggest an element of chronic pulmonary hypertension resulting from a potentially diverse group of etiologic possibilities (e.g., chronic thromboembolic pulmonary hypertension, left ventricular failure, valvular disease, right-to-left cardiac shunts).

DIAGNOSIS OF DEEP VENOUS THROMBOSIS AND PULMONARY EMBOLISM

History and Physical Examination

The presence of erythema, warmth, pain, swelling, and/or tenderness are not specific for DVT but suggest the need for further evaluation. PE must always be considered when unexplained dyspnea is present. Pleuritic chest pain and hemoptysis are also common in PE. Coughing may be present, and while sometimes caused by PE, it more commonly occurs with bronchitis or pneumonia. Anxiety and light-headedness are symptoms that may be caused by PE but may also be caused by a number of other entities that result in hypoxemia or hypotension. Severe dyspnea and syncope are the principal

symptoms that may suggest massive, life-threatening PE. Tachypnea and tachycardia are the most common signs of PE, but they are also nonspecific. A pleural rub or accentuated pulmonic component of the second heart sound may suggest PE, but can also be explained by other disorders. With embolism of sufficient magnitude to cause right ventricular dysfunction, a murmur of tricuspid regurgitation, systemic hypotension, or jugular venous distension might be present.

A major advance in the diagnostic approach to both venous thrombosis and pulmonary embolism has been a transition from a technique-oriented approach to one that utilizes Bayesian analysis. In doing so, the pretest probability of the disease, calculated independently of a particular test result through either empiric means or through a standardized prediction rule, is calculated. This pretest probability aids in the selection and interpretation of further diagnostic tests to create a posttest probability of the disease.

This posttest probability can then be used as a basis for clinical decision making. For pulmonary embolism, three such scores have been developed and validated.

Wells and coworkers prospectively tested a rapid seven-item bedside assessment to estimate the clinical pretest probability for PE.[20] An alternative scoring system, the Geneva score, involved seven variables and required gas exchange and radiographic information. Recently, a revised Geneva score requiring eight clinical variables without gas exchange or radiographic information was validated and published.

Although such scoring systems have not proven to be more accurate than implicit assessment, they do provide a means of standardization that compensates for variability in physician experience and judgment.

DIFFERENTIAL DIAGNOSIS

PE may mimic a large spectrum of diseases. The most common differential diagnoses are chronic lung disease, asthma, congestive heart failure, pneumonia, acute myocardial infarction, aortic dissection, primary pulmonary hypertension, chronic thromboembolic hypertension, pericarditis, cancer, pneumothorax, costochondritis, musculoskeletal pain, and anxiety states.

NONIMAGING STUDIES FOR PULMONARY EMBOLISM

D-Dimer

The plasma D-dimer is a specific derivative of cross-linked fibrin. Measurement of circulating plasma D-dimer has been comprehensively evaluated as a diagnostic test for acute VTE. A normal enzyme-linked immunosorbent assay (ELISA) is highly sensitive in excluding PE and DVT. An increased D-dimer level is nonspecific for PE and may be seen with advancing age and in patients with various diseases, including infections and other inflammatory states, cancer, myocardial infarction, the postoperative state, and second- and third-trimester pregnancies.

ARTERIAL BLOOD GAS ANALYSIS

An important tenet should be that unexplained hypoxemia, particularly in the setting of risk factors for DVT, suggests the possibility of PE.

ELECTROCARDIOGRAPHY

ECG findings in acute PE are generally nonspecific and include T-wave changes, ST-segment abnormalities, incomplete or complete right bundle-branch block, right axis deviation in the extremity leads, and clockwise rotation of the QRS vector in the precordial leads. The changes that do occur are likely caused by right-heart dilatation.

Approximately 20 percent of patients with PE have no electrocardiographic changes.

The "classic" S1 Q3 T3 pattern described by McGinn and White in 1935 in seven patients with acute cor pulmonale secondary to PE was subsequently demonstrated to be present in approximately 10 percent of PE cases.[21,22]

In patients without underlying cardiac or pulmonary disease from the Urokinase Pulmonary Embolism Trial (UPET), ECG abnormalities were documented in 87 percent of patients with proven PE. In this clinical trial, 26 percent of patients with massive or submassive PE and 32 percent of those with massive PE[23] had manifestations of acute cor pulmonale, such as the S1 Q3 T3 pattern, right bundle-branch block, a P-wave pulmonale, or right axis deviation. The low frequency of specific ECG changes associated with PE was confirmed in the PIOPED study.

Despite its lack of diagnostic accuracy, ECG may be helpful in predicting adverse clinical outcomes in patients with PE. It was recently suggested that a T-wave inversion in V2 or V3 is the most frequent ECG sign of massive PE. In another PE study, both the pseudoinfarction pattern (Qr in V1) and T-wave inversion in V2 were closely related to the presence of right ventricular dysfunction and were independent predictors of adverse clinical outcome.[24]

IMAGING STUDIES FOR PULMONARY EMBOLISM

Chest Radiography

The chest radiograph is abnormal in the majority of patients with PE, but the findings are nonspecific and often subtle. Atelectasis, cardiomegaly, pulmonary infiltrates, small pleural effusions, and mild elevation of a hemidiaphragm may be present.

Classic radiographic evidence of pulmonary infarction (Hampton hump) or decreased vascularity (Westermark sign) are suggestive but uncommon. A normal chest radiograph in the presence of significant dyspnea and hypoxemia without evidence of bronchospasm or anatomic cardiac shunt is strongly suggestive of PE.

COMPUTED TOMOGRAPHY OF THE CHEST

Contrast-enhanced computed tomography (CT) of the chest has become the most useful imaging test in patients with clinically suspected acute PE.

First-generation scanners have poor resolution in the segmental pulmonary arteries and a limited sensitivity for subsegmental clots. However, they appear to predict a benign clinical course over the ensuing 3 months.[25,]

Second-generation scanners involve continuous movement of the patient through the scanner with concurrent scanning by a constantly rotating gantry and detector system. A helix of projecting data is obtained. Continuous volume acquisitions can be obtained during a single breath. Rapid scans can be obtained, facilitating imaging in critically ill patients.

The latest generation of multidetector-row CT scanners permits image acquisition of the entire chest with 1-mm or submillimeter resolution with a breathhold of less than 10 seconds.[26,27] The latest generation of 64-slice scanners can image thrombus in sixth-order vessels.

An additional advantage is evaluating a patient for the entire spectrum of VTE in one imaging session by scanning the legs and pelvis, as well as the lungs.

Outcome studies have demonstrated that embolism can be safely excluded using a clinical assessment tool, D-dimer testing, and computed tomography except in those patients who present with a high clinical likelihood of embolism.

VENTILATION–PERFUSION SCANNING

V/Q scanning has been the pivotal diagnostic test for suspected PE for many years. Chest CT has now virtually replaced lung scanning.

PULMONARY ANGIOGRAPHY

Standard contrast pulmonary arteriography is the established "gold standard" imaging test for the diagnosis of PE.

Prior to injecting contrast agents into the pulmonary artery, optimal recording of right-heart pressure tracings is important. If pressure curves "wedge" in the main pulmonary arteries, massive PE should be suspected. If the mean pulmonary artery pressure exceeds 40 mmHg, preexisting pulmonary hypertensive disorders, including chronic thromboembolic pulmonary hypertension, should be included in the differential diagnosis.

The primary sign for PE is an intraluminal filling defect in an arterial branch or cutoff of a branch with the visualized tail of the embolus Secondary signs of PE are decreased abrupt occlusion of a vessel, oligemia or avascularity, prolonged arterial phase with slow filling and emptying of veins, and tortuous peripheral vessels.

In chronic pulmonary hypertension, the pulmonary arteries are pouched and contain organized thrombi with usually concave edges. Bands and webs within the arteries may be present. Lobar and segmental vessels may show abrupt narrowing or occlusion.

MAGNETIC RESONANCE IMAGING

Gadolinium-enhanced magnetic resonance (MR) angiography is also being used to evaluate clinically suspected PE.[28,29]

A more recent study showed that when MR is performed under optimal conditions, it appears to be highly sensitive and specific even for segmental PE in comparison to pulmonary angiography.

ECHOCARDIOGRAPHY

Transthoracic echocardiography has emerged as a potentially important tool for risk assessment and treatment guidance in patients with acute PE. The presence of right ventricular dysfunction on a baseline echocardiogram in normotensive patients appears to represent an independent predictor of an adverse outcome or early death.

However, approximately 40 percent of normotensive patients with symptomatic pulmonary embolism will have echocardiographic evidence of right ventricular dysfunction and it remains controversial whether all such patients, the majority of whom will do well with conventional therapy, should be subjected to the risks of thrombolytic therapy.

Right ventricular systolic dysfunction in routine clinical practice is semiquantitatively assessed by examination of the right ventricular free wall motion using a four-point scale normal/near-normal right ventricular function and mild, moderate, or severe right ventricular dysfunction. Patients with severe right ventricular dysfunction may show regional wall motion abnormalities of the right ventricle known as the ***McConnell sign-*** evidence of severe hypokinesis of the right ventricular free wall combined with preserved systolic contraction of the right ventricular apex.[30]

Right ventricular dilatation is an indirect sign of right ventricular pressure overload in the setting of acute PE. The ratio of right ventricular to left ventricular size should be measured using M-mode echocardiography in the parasternal long-axis view at the level between the mitral valve and the papillary muscle. An alternative is to measure the size ratio of both ventricles in the apical four-chamber view at the level of the atrioventricular valves. A ratio of right ventricular to left ventricular size of 1 in the apical four-chamber view and 0.5 in the parasternal long-axis view indicates right ventricular dilation. In patients with severe right ventricular pressure overload, a constant shift of the interventricular septum toward the left ventricle or a paradoxical (systolic) septal movement toward the left ventricle may be observed. In the parasternal short-axis view, a constant shift of the septum to the left side often causes a "D-shaped" left ventricle

Further indirect signs of right ventricular dysfunction are systolic pulmonary artery hypertension manifested by an increased tricuspid regurgitant velocity >2.6 m/s and reduced inspiratory collapse of a dilated inferior vena cava because of elevated central venous pressure.

DIAGNOSTIC STRATEGY

The overall diagnostic approach depends on the hemodynamic presentation of the patient.

While rapid diagnosis and therapeutic intervention is required in patients with shock and suspected massive PE, there is sufficient time to obtain imaging tests in hemodynamically stable patients with suspected PE.

PATIENTS WITH SUSPECTED PULMONARY EMBOLISM AND SHOCK

In patients with hypotension or cardiogenic shock associated with suspected massive PE, rapid initiation of therapy is potentially lifesaving. The definition of massive pulmonary embolism should be based on hemodynamic considerations rather than purely anatomic considerations. Irrespective of the degree of vascular obstruction, patients with pulmonary embolism who present with shock have a mortality rate that approaches 30 percent, whereas those suffering a cardiopulmonary arrest have a mortality rate that approximates 70 percent.

Time-consuming imaging tests often can be avoided when emergency bedside echocardiography is available. In patients with suspected massive PE and evidence of severe acute right ventricular dysfunction on the echocardiogram, thrombolysis or embolectomy may be rapidly initiated. A caveat to this general recommendation exists in patients presenting with decompensated right-heart failure caused by nonembolic forms of pulmonary hypertension.

Clues to the chronic nature of the right ventricular dysfunction would be a history of chronic rather than acute dyspnea, the presence of right ventricular hypertrophy rather than simple dilatation, or estimated pulmonary artery systolic pressures by echocardiogram greater than approximately 70 mmHg.

PATIENTS WITH SUSPECTED PULMONARY EMBOLISM WITHOUT SHOCK

Pulmonary embolism cannot be excluded without objective testing. The history, physical examination, and diagnostic studies, such as a chest radiograph, electrocardiogram, or arterial blood gas analysis, can raise or lower the clinical suspicion of embolism but are incapable of excluding or confirming it unless a clearly identifiable condition (e.g., strategies have been investigated and algorithms constructed capable of confirming or excluding the diagnosis of embolism under most circumstances.

In all emergency room or other outpatients, the clinical pretest probability for PE should be calculated by implicit assessment or, preferably, through a standardized technique.

A highly sensitive plasma D-dimer assay such as an ELISA should be obtained. Unless the pretest probability is high, pulmonary embolism can be excluded by a D-dimer result below the assay-specific cutoff level. In patients with elevated D-dimer levels or a high clinical probability of embolism, spiral chest CT should be obtained. In patients with significant impairment of renal function, pregnancy, or allergy to contrast agents, lower-extremity duplex study, or ventilation–perfusion scanning may be preferred as the primary chest imaging test.

Diagnostic strategy for patients with suspected pulmonary embolism (PE) without shock.

In this strategy, chest computed tomography is used as the principal imaging test

Further testing should be considered if the test is inconclusive or negative, with a persistent suspicion of PE.

The approach to a hospitalized patient with suspected embolism is different. At the present time, the safe exclusion of embolism in inpatients using a clinical prediction rule and D-dimer result remains to be established. D-Dimer testing has little clinical utility in inpatients because of its poor specificity.

At the present time, embolism can be safely excluded in patients with a low or intermediate probability of embolism by a normal, highly-sensitive D-dimer assay, a normal or near-normal ventilation–perfusion scan, a negative CT angiogram, or a negative contrast angiogram. In patients with a high probability of embolism, clinical outcome appears to be acceptable following a negative CT angiogram and lower-extremity duplex examination, but definitive exclusion requires either a normal ventilation–perfusion scan or a negative contrast pulmonary angiography. Under this circumstance, clinical judgment must come into play with the risk of possible recurrence balanced against the risk of additional diagnostic procedures.

Embolism can be confirmed in patients with an intermediate or high probability of embolism by a high probability ventilation–perfusion scan, a positive CT angiogram, or a positive lower-extremity duplex examination. In patients with a low probability of embolism, pulmonary angiography is required unless a CT angiogram is positive.

MANAGEMENT

Risk Stratification

Transthoracic echocardiography is the most important tool for risk stratification because right ventricular dysfunction on the echocardiogram is a powerful and independent predictor of mortality. From a prognostic point of view, echocardiography helps to classify PE into three groups:

(1) Low-risk PE **(**no right ventricular dysfunction) with a hospital mortality of <4 percent,

(2) Submassive PE (right ventricular dysfunction and a preserved systemic arterial pressure) with a hospital mortality of 5 to 10 percent, and

(3) Massive PE (right ventricular dysfunction and cardiogenic shock) with a hospital mortality of approximately 30 percent

CARDIAC BIOMARKERS

Troponins and natriuretic peptides are similarly accurate in identifying low-risk PE patients.[31,32] The negative predictive value for inhospital death is high for the biomarker assays The cutoff levels for troponins are the lower detection limits for myocardial ischemia reported by the manufacturer. In one clinical trial, the cutoff level for the brain natriuretic peptide triage assay to predict a benign clinical outcome in PE patients was lower (<50 pg/mL) than the "congestive heart failure" cutoff level of 90 pg/mL.[33]

Cumulative survival rate at 30 days in patients with acute pulmonary embolism according to the level of troponin T. A level >0.1 ng/mL identifies patients at high risk for adverse clinical outcome.

ANTICOAGULATION

Standard Unfractionated Heparin Unfractionated heparin (UFH) is a highly sulfated glycosaminoglycan . Heparin acts primarily by binding to antithrombin III (AT III), a protein that inhibits the coagulation factors thrombin (factor IIa), Xa, IXa, XIa, and XIIa.accelerates its activity approximately 100- to 1000-fold.

This prevents additional thrombus formation and permits endogenous fibrinolytic mechanisms to lyse clot that has already formed.

Heparin does not directly dissolve thrombus that already exists.

Heparin is the cornerstone of treatment for acute PE. Before starting heparin, evaluate potential risk factors for bleeding, such as a prior history of bleeding with anticoagulation, thrombocytopenia, vitamin K deficiency, increasing age, underlying diseases, and concomitant drug therapy

When intravenous unfractionated heparin is instituted, the activated partial thromboplastin time (aPTT) should be aggressively followed at 6-hour intervals until it is consistently in the therapeutic range of 1.5 to 2.0 times control values. Heparin can be administered as an intravenous bolus of 5000 U followed by a maintenance dose of at least 30,000 U every 24 hours by continuous infusion.[34] An alternative regimen consisting of a bolus of 80 U/kg followed by 18 U/kg/h has been recommended.[35,36] Subsequent dose modifications, based on aPTT as follows:

a. APTT Heparin Dose Adjustment

b. Seconds Times Control

c. <35 <1.2 80 U/kg bolus, then increase by 4 U/kg/h

d. 35 to 45 1.2 to 1.5 40 U/kg bolus, then increase by 2 U/kg/h

e. 46 to 70 1.5 to 2.3 No change

f. 71 to 90 2.3 to 3 Decrease infusion rate by 2 U/kg/h

g. >90 >3 Hold infusion 1 h, then decrease rate by 3 U/kg/h

UPPER-EXTREMITY DVT

Effort-related upper-extremity venous thrombosis **(Paget-Schroetter syndrome)** affects young, active men and is related to extrinsic compression of the subclavian vein at the thoracic inlet. A multidisciplinary approach to management is often required to avoid long-term consequences including recurrence, embolism, and symptomatic sequelae.[37]

Potential Advantages of Low-Molecular-Weight Heparins over Unfractionated Heparin

1) Efficacy: comparable or superiora
2) Safety: comparable or superiorb
3) Bioavailability: superior
4) Subcutaneous administration
5) Once- or twice-daily dosing
6) No laboratory monitoring
7) Less phlebotomy
8) Earlier ambulation
9) Home therapy in certain patient subsets

LMWH

Enoxaparin 30 mg q12h or 40 mg qd 1 mg/kg bid, 1.5 mg/kg qda

Dalteparin 2500 to 5000 Xa U qd 200 Xa U/kg qd

Enoxaparin is the only LMWH approved for use in the United States It is indicated in patients who present with DVT (with or without concomitant pulmonary embolism [PE]). A dose of either 1.5 mg/kg or 1 mg/kg q12h has proven effective for inpatients with DVT ± PE.

Optimal Duration and Intensity of Anticoagulation

Patients with a clearly defined initial predisposition, whose initial thromboembolic risk factors have resolved and whose ventilation–perfusion scan and noninvasive lower-extremity testing have normalized, can be managed with a 3-month course of anticoagulation.

Patients without a clearly defined initial predisposition to abnormal lower-extremity test results should be treated for 6 months or more.

Patients, such as those with recurrent spontaneous episodes of venous thromboembolism, an irreversible clinical risk factor, combined thrombophilic tendencies, antithrombin III deficiency, or the presence of a lupus anticoagulant, should be treated with an indefinite period of anticoagulation even though such a strategy is associated with an increased risk of bleeding complications.

Vena Cava Interruption

In patients with established VTE in whom heparin therapy cannot be continued, inferior vena cava (IVC) filter placement can be undertaken to prevent lower-extremity thrombi from embolizing to the lungs.[38]

Greenfield filter design is the most widely used.[39]

THROMBOLYTIC THERAPY

Systemic Thrombolysis

The role of thrombolytic therapy in pulmonary embolism should be limited to those circumstances in which an accelerated rate of thrombolysis with hemodynamic compromise, patients who develop hemodynamic compromise during conventional therapy with heparin, and patients with embolism associated with intracavitary right-heart thrombi.

At the present time, the finding of right ventricular dysfunction on echocardiography in the absence of hemodynamic instability should not serve as a justification for routine thrombolytic therapy.

There are only 10 randomized PE trials of thrombolysis versus heparin to date, with a total of 717 patients with varying severity of PE. In an overview, there is a trend toward mortality reduction with thrombolysis.[40-46]

None of the thrombolytic agents have been shown to be superior to the others. FDA-approved thrombolytic agents include recombinant tissue plasminogen activator, streptokinase, and urokinase. presents thrombolytic regimens for the treatment of PE.

REGIMENS FOR SYSTEMIC THROMBOLYTIC THERAPY IN PULMONARY EMBOLISM

Lytic Agent Dose Regimen

Streptokinase Loading dose: 250,000 U IV

Continuous infusion: 100,000 U/h for 24 h

Urokinase Loading dose: 2000 U/lb IV over 10 min

Continuous infusion: 2000 U/lb/h for 12–24 h

Alteplase (tPA) Loading dose: none

Continuous infusion: 100 mg over 2 h

Reteplase 1. Bolus: 10 U IV

2. Bolus: 10 U IV after 30 min

tPA, tissue plasminogen activator.

Heparin should be withheld until the thrombolytic infusion is completed. The aPTT is then determined and heparin is initiated without a loading dose if this value is less than twice the upper limit of normal. If the aPTT exceeds this value, the test is repeated every4 hours until it is safe to proceed with heparin.

It is reasonable to consider systemic thrombolytic therapy in patients with proximal occlusive DVT associated with significant swelling and symptoms when there are no contraindications.

CATHETER FRAGMENTATION AND EMBOLECTOMY

Interventional thrombus fragmentation with or without embolectomy is an alternative to systemic thrombolysis or surgical embolectomy. If the bleeding risk is not exceedingly high, catheter fragmentation may be combined with local or systemic thrombolysis.

SURGICAL EMBOLECTOMY

Acute embolectomy might be considered in patients with hemodynamically massive pulmonary embolism or right-heart thrombus who have an absolute contraindication to anticoagulant or thrombolytic therapy, in patients who have suffered a cardiopulmonary arrest (although the mortality associated with embolectomy in those who have experience arrest is far higher than those who have not), in patients with impending paradoxical embolism, and in patients in whom aggressive medical therapy, including the use of thrombolysis, has proven ineffective.

SUPPORTIVE MEASURES

When massive PE associated with hypotension and/or severe hypoxemia is suspected, supportive treatment is immediately initiated. Intravenous saline can be infused rapidly, but caution is recommended. Excess fluid can result in further right ventricular dilatation, increased right ventricular wall tension, and a decreased cardiac output that may result in right ventricular ischemia. Dopamine or norepinephrine appear to be the favored choices of vasoactive therapy in massive PE and should be administered if the blood pressure is not rapidly restored. Death from massive PE results from right ventricular failure, and dobutamine has been recommended by some as a means by which to augment right ventricular output[47,48] might offer optimal results. Mechanical ventilation may be instituted to decrease systemic oxygen demands or to manage respiratory failure. Intubation in the setting of a decompensated right ventricle, however, is fraught with risk. Premedications may cause systemic vasodilatation,

whereas positive pressure ventilation may abruptly reduce preload and cardiac output.

CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION

In a few patients with acute PE, the residual thromboembolic burden is sufficiently extensive to cause thromboembolic pulmonary hypertension. A variety of CT abnormalities have been described in patients with chronic thromboembolic disease including right-sided cardiac enlargement, enlargement of the pulmonary arteries, a mosaic perfusion pattern, intraluminal thrombus, subpleural densities, and dilated bronchial arteries.[49] The absence of these findings, however, cannot absolutely exclude the diagnosis.

Following acute embolism, stable hemodynamics are achieved within 6 to 8 weeks.[50] Consequently, to avoid the possible development of a secondary, small-vessel arteriopathy that ultimately contributes to the elevation in pulmonary vascular resistance and which is not amenable to surgical correction, there is no need to delay evaluation beyond 3 months. Right-heart catheterization and contrast pulmonary arteriography are performed to establish the diagnosis with certainty and to determine operability. The angiographic findings in chronic thromboembolic pulmonary hypertension are distinct from those encountered in acute embolism and considerable experience is required for accurate angiographic interpretation

MATERIAL AND METHODS

This study was performed in the Department of Cardiology, Rajiv Gandhi Government General Hospital, Chennai, during the year 2008 – 2011. The study is a prospective observational study involving 50 patients.

STUDY GROUP SELECTION

Ethical committee clearance was obtained to conduct the study in our hospital.

All subjects provided written informed consent to participate in the study before inclusion.

50 consecutive patients with symptoms of

unexplained dyspnoea

chest pain

fainting,

ECGor ECHO signs of acute corpulmonale

were taken as cases of suspected PE.

All the patients underwent ,physical exam, ECG,ECHO d-dimer assay, CT pulmonary angiogram and other relevant examinations.

All the patients underwent, probability of PE assessment for Pisa, Wells, and Revised Geneva Model. They were categorized into low, intermediate , high in each score as per the criteria in each category

PISAMODEL

Sex	
Age	
Immobilization	
Deep vein thrombosis	
Cardiovascular Pre-existing disease	
Pulmonary Pre-existing disease	
Dyspnoea (Sudden- onset)	
Orthopnea	
Chest pain	
Fainting(syncope)	
Hemoptysis	
Leg Swelling(Unilateral)	
Fever>38^0 C (>100.4^0F)	
Wheezes	
Crackles	
Acute Corpulmonale in ECG	

PROBABILITY OF PE IN PISA MODEL

LOW:	0-10%
INTERMEDIATE:	11-50%
HIGH	>50%

WELLS SCORE

PREDISPOSING FACTORS	*POINTS*
PREVIOUS DVT OR PE	+1.5
RECENT SURGERY OR IMMOBILISATION	+1.5
CANCER	+1
SYMPTOMS	
HEMOPTYSIS	+1
CLINICAL SIGNS	
HEART RATE>100/MIN	+1.5
CLINICAL SIGN OF DVT	+3
CLINICAL JUDGEMENT	
ALTERNATE DIAGNOSIS LESS LIKELY THAN PE	+3

CLINICAL PROBABILTY (3 –LEVEL) WELLS	**TOTAL**
LOW	0 TO 1
INTERMEDIATE	2 TO 6
HIGH	≥ 7

REVISED GENEVA SCORE

PREDISPOSING FACTORS	*POINTS*
AGE>65 YRS	+1
PREVIOUS DVT OR PE	+3
SURGERY OR FRACTURE IN 1 MONTH	+2
ACTIVE MALIGNANCY	+2
SYMPTOMS	
UNILATERAL LOWER LIMB PAIN	+3
HEMOPTYSIS	+2
CLINICAL SIGNS	
HEART RATE	
75 TO 94 /MIN	+3
≥94 /MIN	+5
PAIN ON LOWER LIMB DEEP VEIN PALPATION AND UNILATERAL EDEMA	+4

CLINICAL PROBABILITY	**TOTAL**
LOW	0 TO 3
INTERMEDIATE	4 TO 10
HIGH	≥11

In each patient, probability of pulmonary embolism is calculated for all the three models-pisa wells and revised geneva score

IN ECG

Following findings were looked in patients for acute corpulmonale

1 T wave inversion v1 – v4

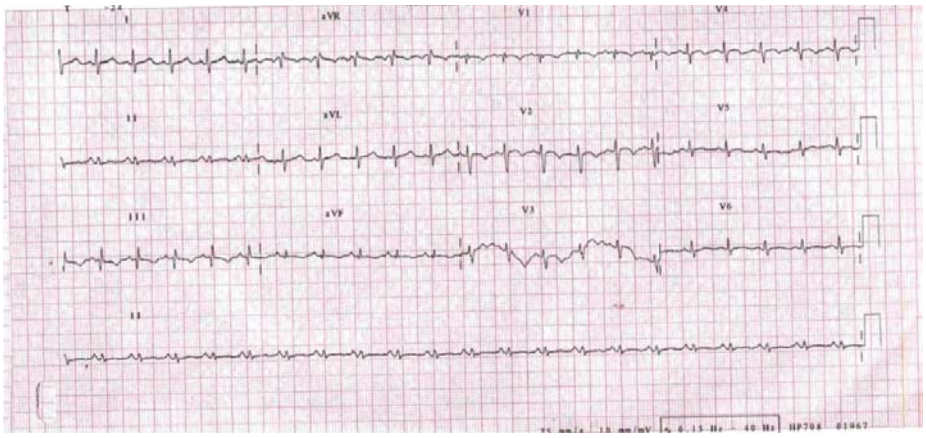
2 Tachycardia

3 S1Q3T3 pattern

4 RBBB

5 Rightaxisdeviation

ECG



ECG from one of the study patient showing classical finding of PE

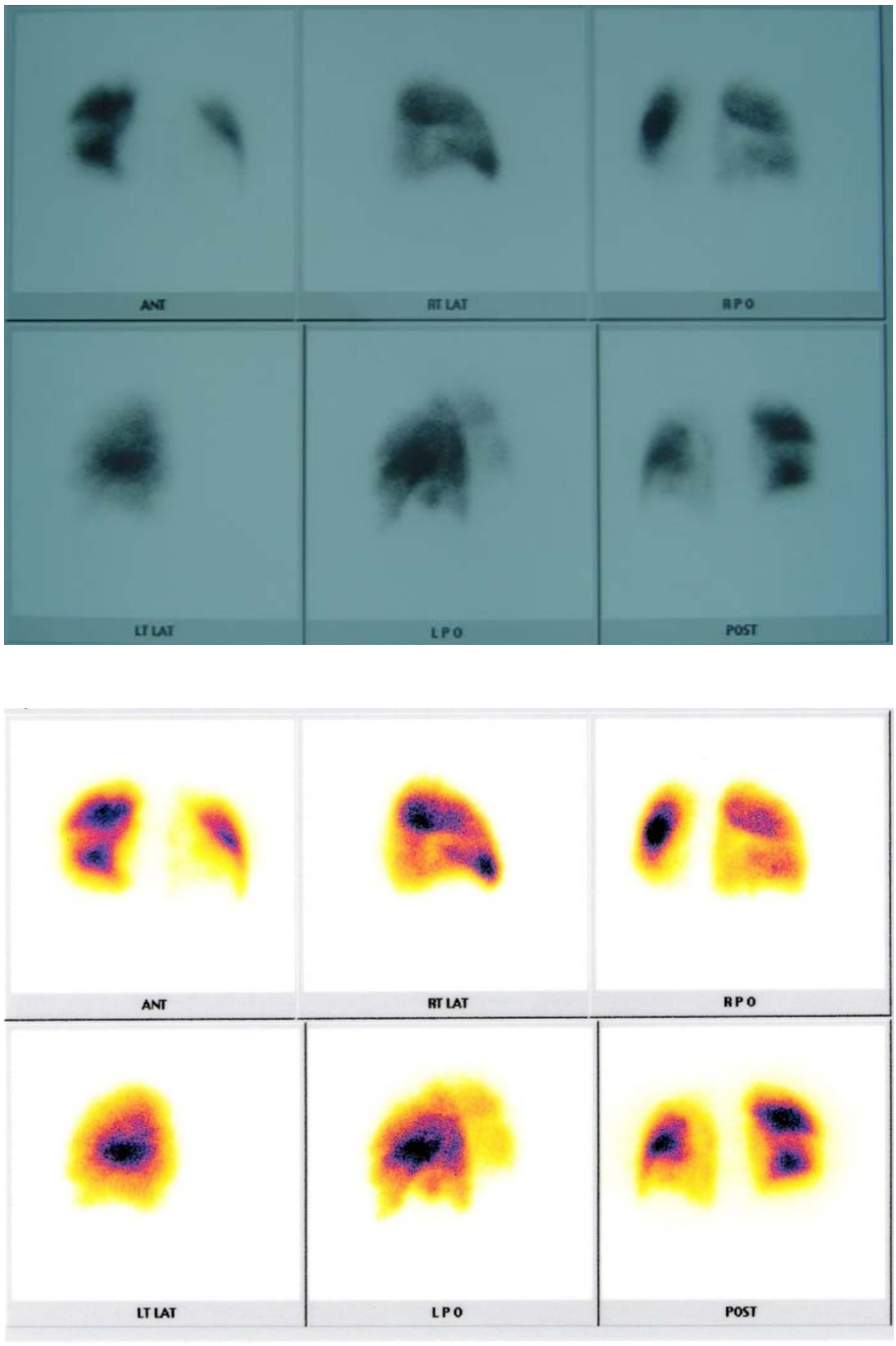
1. S1Q3T3

2. Tachycardia

3. RV Strain

4. incomplete RBBB

VENTILATION-PERFUSION SCAN



Ventilation –perfusion scan from one of our study patient showing mis-match

ECHOCARDIOGRAPHY

Echocardiography was done immediately in all the patients by Philips Envisor which produces good imaging quality

Following specific findings were looked in the ECHO

RA RV dilatation.

A constant shift of the interventricular septum toward the left ventricle or a paradoxical (systolic) septal movement toward the left ventricle

"D-shaped" left ventricle

Increased tricuspid regurgitant velocity >2.6 m/s

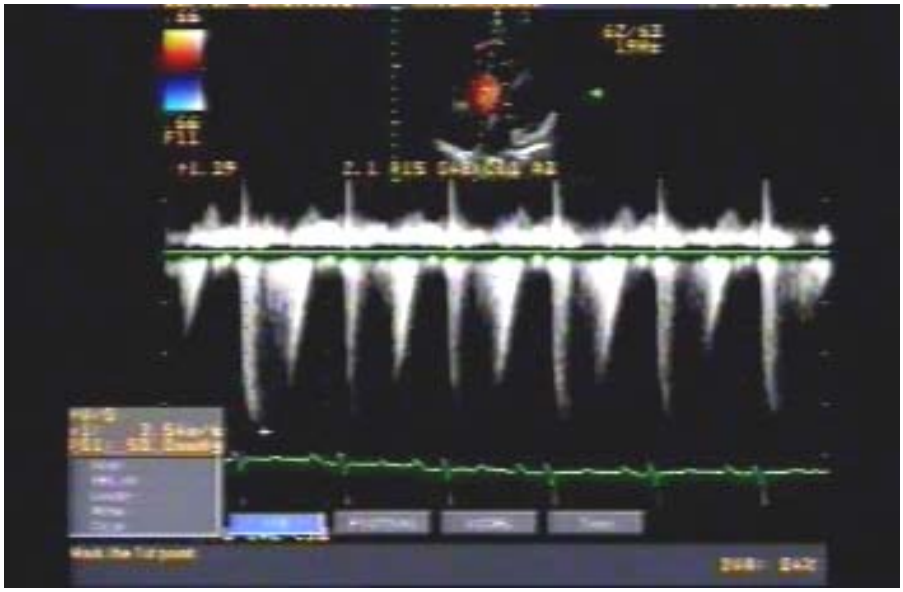
Reduced inspiratory collapse of a dilated inferior vena cava

McConnell sign: evidence of severe hypokinesis of the right ventricular free wall combined with preserved systolic contraction of the right ventricular apex

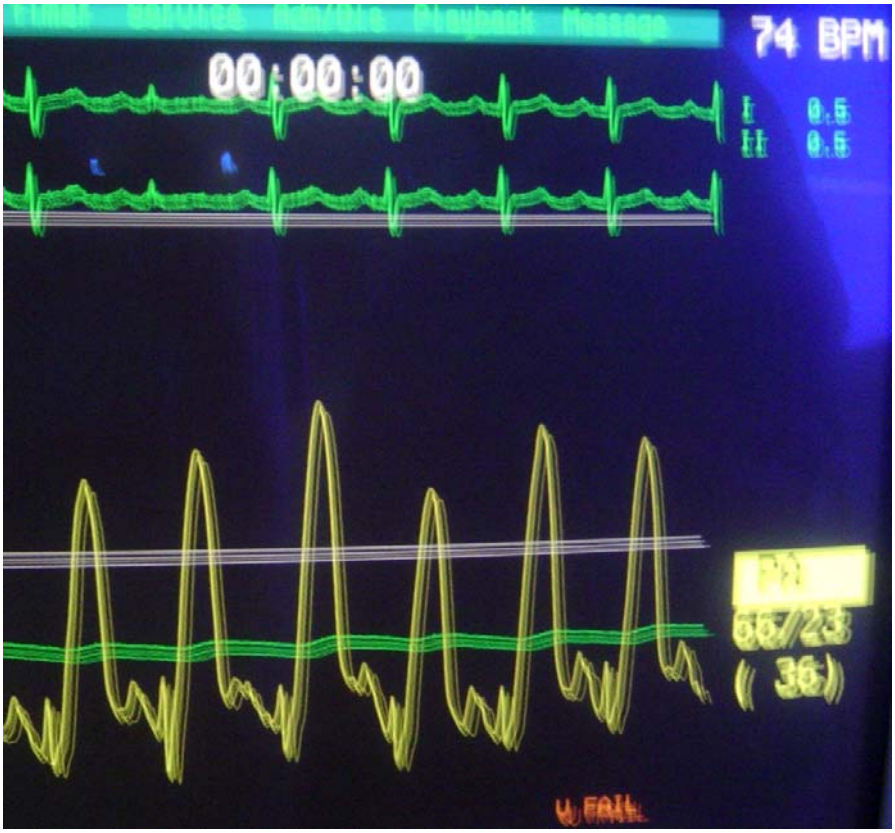
Shortened PA acceleration time less than 60-100 ms particularly in the presence of RVsystolic pressure less than 60 mm Hg-specific for acute PE

D Shaped septum

RA RV Dilatation



TR PG 50 mmHg



PULMONARY ARTERY PRESSURE –66/23-MEAN 36

PULMONARY ARTERY PRESSURE TRACING OF PE IN ONE OF OUR PATIENT

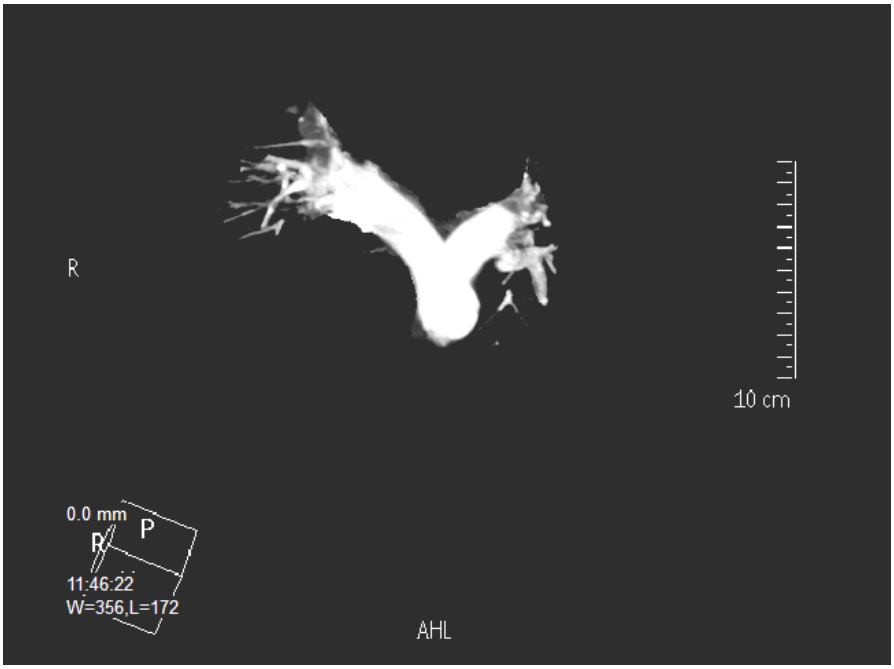
64-SLICE CT PULMONARY ANGIOGRAM

64 Slice CT Pulmonary Angiogram is done for all patients to confirm presence or absence of PE as per the current methodology

It is done in all the patients before Thrombolysis in our radiology department which is adjacent to our department

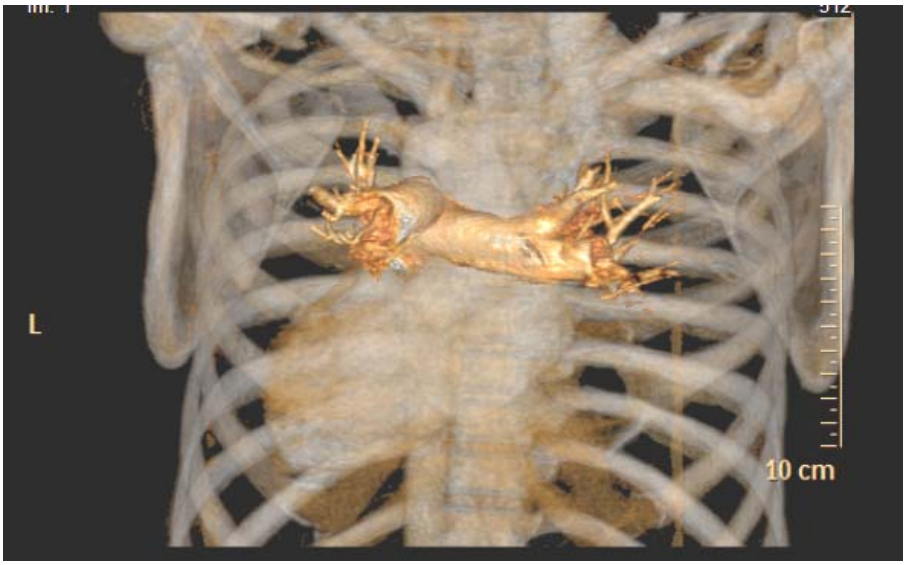
The primary sign for PE is an intraluminal filling defect in an arterial branch or cutoff of a branch with the visualized tail of the embolus

Secondary signs of PE are decreased abrupt occlusion of a vessel, oligemia or avascularity of a segment



Pulmonary Angiogram Showing filling defect and poor peripheral vascular blood supply with cut off sign.

Dilated pulmonary artery and filling defect.



64-Slice CT Pulmonary Angiogram showing filling defect and poor peripheral vascular blood supply with cut off sign.

RESULTS

Patient Characteristics

Total number of patients 50

In the age group15-56 35 patients, 57-67 14 patients, 68-74 1patient

In the study group 38 patients were males and 12 patients were females

20 patients were proven to have pulmonary embolism.

The most common symptom was sudden onset dyspnoea in 15 patients

History of immobilization found in 8 patients.

DVT was found in 9 patients

RV strain in ECG was found in 10 patients

S1Q3 pattern in ECG was found in 11 patients

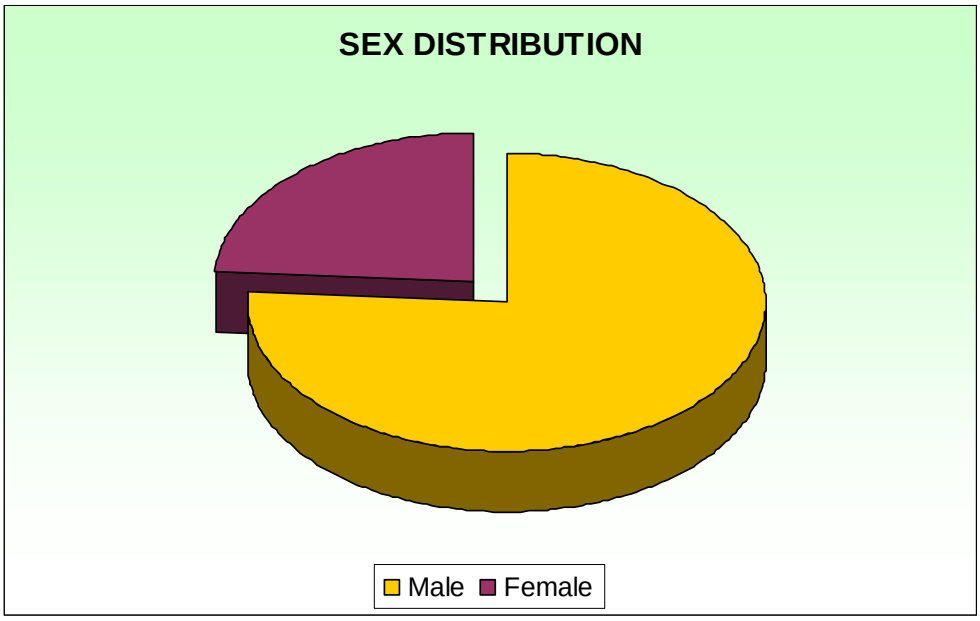
ECHO showed RV enlargement in 12 patients

TR PG greater than 40 mm Hg was found in 14 patients

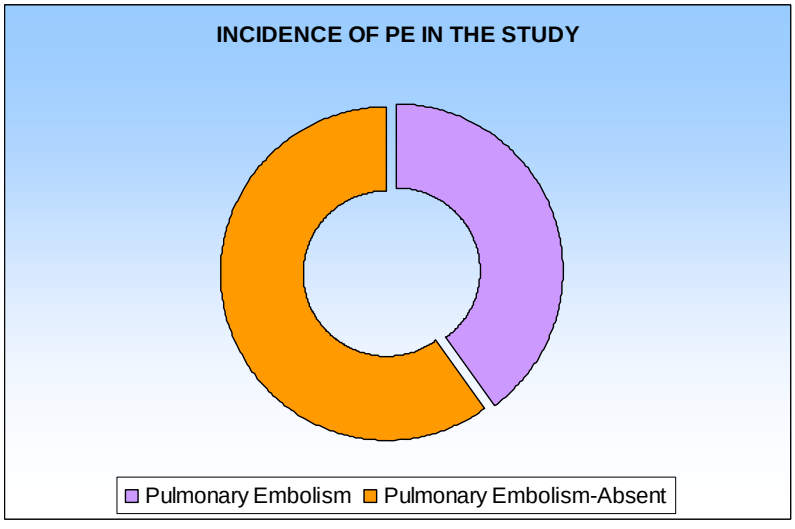
PATIENT CHARACTERISTICS

PATIENT CHARACTERISTICS	NO. OF PATIENTS	PERCENTAGE (%)
Age		
15-56	35	**70%**
57-67	14	**28%**
68-74	1	**2%**
75-94	0	**0%**
Gender		
Male	38	**76%**
Female	12	**24%**
DVT	9	**45%**
RV strain in ECG	10	**50%**
S1Q3 pattern	11	**55%**
RV enlargement	12	**60%**
TR PG	14	**70%**
Pulmonary Embolism	20	**40%**

In the study group 38 patients were males and 12 patients were females.



20 patients were proven to have pulmonary embolism



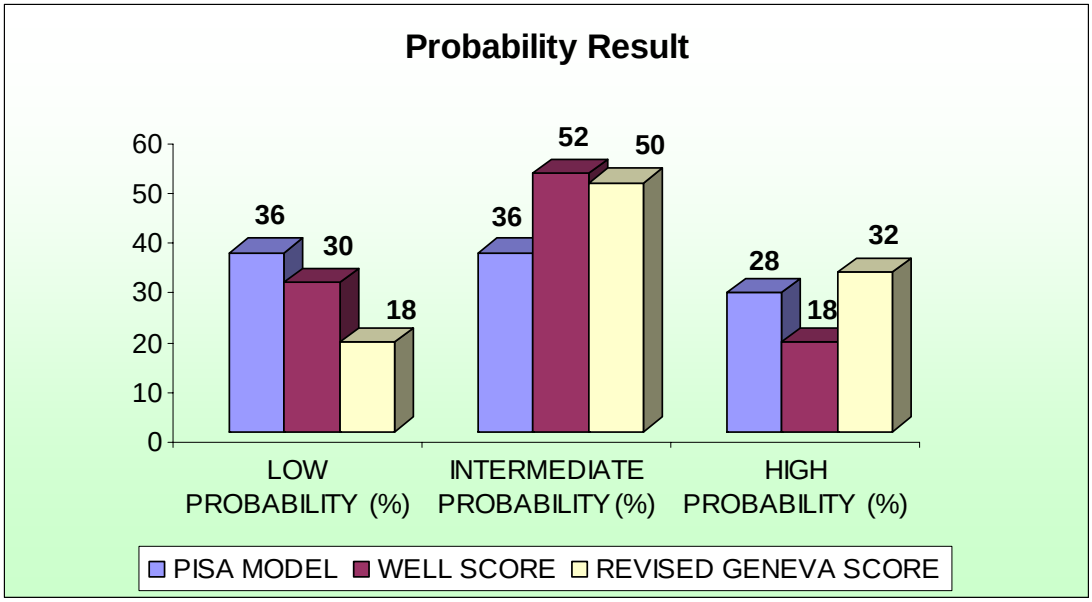
Among 50 patients Pisa Model has predicted low probability in 36%, intermediate probability in another 36% and high probability in 28%

Among 50 patients Wells Model has predicted low probability in 30%, intermediate probability in another 52% and high probability in 18%

Among 50 patients Geneva Model has predicted low probability in 18% , intermediate probability in another 50% and high probability in 32%.

PERCENTAGE OF PROBABILITY OF PE

MODEL	***LOW PROBABILITY (%)***	***INTERMEDIATE PROBABILITY (%)***	***HIGH PROBABILITY (%)***
PISA MODEL	36	36	28
WELL SCORE	30	52	18
REVISED GENEVA SCORE	18	50	32



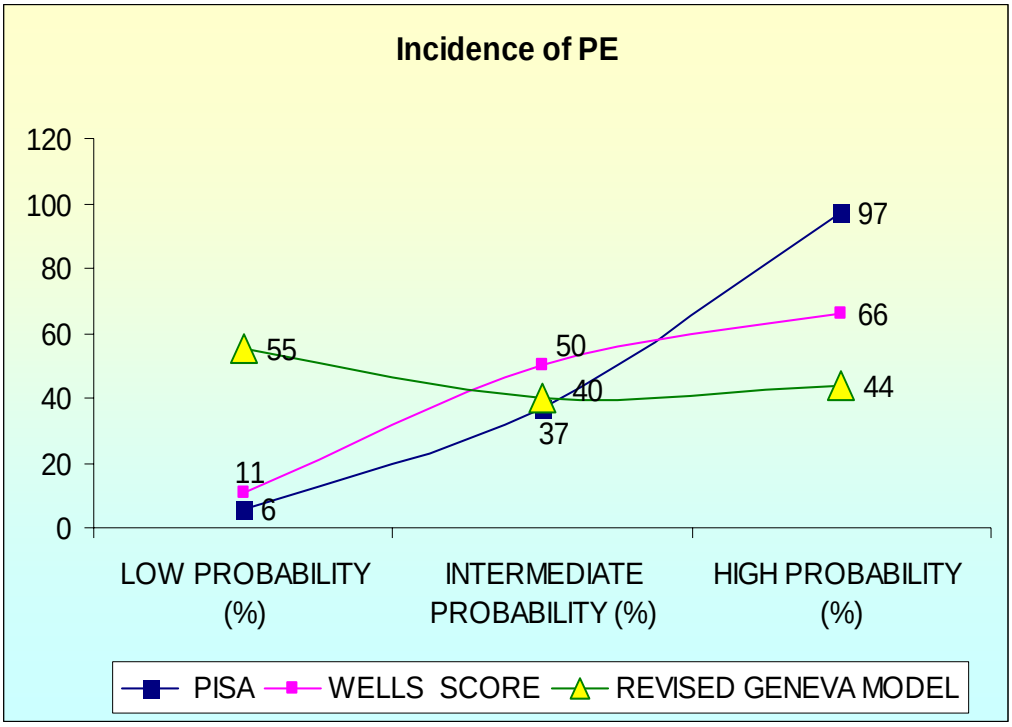
INCIDENCE OF PULMONARY EMBOLISM

MODEL	LOW PROBABILITY (%)	INTERMEDIATE PROBABILITY (%)	HIGH PROBABILITY (%)
PISA	6	37	97
WELLS SCORE	11	50	66
REVISED GENEVA MODEL	55	40	44

In Pisa Model when the probability is low there was 1 case of PE, when it is intermediate there were 6 cases and when the probability is high there were 13 cases

In Wells Model when the probability is low there were 2 cases of PE, when it is intermediate there were 13 cases and when the probability is high there were 5 cases

In Revised Geneva Model when the probability is low there were 5 cases of PE, when it is intermediate there were 10 cases and when the probability is high there were 5 cases



Comparison of incidence of pulmonary embolism after calculating probability from WELLS SCORE PISAMODEL AND REVISED GENEVA SCORE was done with chi square test.

PISA MODEL

	PE	***Low***	***Intermediate***	***High***	***Pearson chi square test***
Pisa model	no	17(94.4%)	12(66.7%)	1(7.2%)	$\chi 2=25.51$ P=0.001***
	yes	1(5.6%)	6(33.3%)	13(92.8%)	

** highly significant *** very high significant

In the above tabular column Pisa Model is shown to be very highly significant in all low, intermediate and high in calculating the probability of pulmonary embolism.

When the probability is high the incidence of pulmonary embolism is nearly above 92%

When the probability is low incidence is less than 6%

Thus the Pisa Model has very good sensitivity and specificity in predicting the probability of presence of PE when the score is high

When the score is low Pisa Model has good sensitivity and specificity in predicting the absence of PE

WELLS MODEL

	PE	Low	Intermediate	High	Pearson chi square test
Well score	no	13(86.7%)	13(50.0%)	4 (45%)	$\chi 2=7.99$ P=0.01**
	yes	2(14.3%)	13(50.0%)	5 (55%)	

** highly significant *** very high significant

In the above tabular column Wells model is shown to be significant in all low, intermediate and high in calculating the probability of pulmonary embolism.

When the probability is high the incidence of pulmonary embolism is nearly 55% only when compared to Pisa Model which has incidence of 92%

When the probability is low incidence is 14% when compared to Pisa Model which has incidence of 5.6%

Thus the **Pisa Model** has very good sensitivity and specificity in predicting the probability of presence of PE when the score is high **than Wells Model**

When the score is low **Pisa Model** has good sensitivity and specificity in predicting the absence of PE **than Wells Model**

REVISED GENEVA SCORE

	PE	***Low***	***Intermediate***	***High***	***Pearson chi square test***
Geneva	No	4(44.4%)	15(60.0%)	11(68.8%)	$\chi 2=1.41$ P=0.49
	yes	5(55.6%)	10(40.0%)	5(31.2%)	

** highly significant *** very high significant

GENEVA model did not show any significance and this model is found to be not useful.

In each low intermediate high all the three scores were assessed for significance and found to be significant.

Low	**Pisa model**	**Well score**	**RGS**	**Pearson chi square test**
Yes	1(5.6%)	2(14.3%)	5(55.6%)	$\chi 2=10.22$ P=0.001***
No	17(94.4%)	13(86.7%)	4(44.4%)	

Intermediate	**Pisa model**	**Well score**	**RGS**	**Pearson chi square test**
Yes	13(92.8%)	6(66.7%)	5(31.2%)	$\chi 2=12.10$ P=0.001***
No	1(7.2%)	3(33.3%)	11(68.8%)	

High	**Pisa model**	**Well score**	**RGS**	**Pearson chi square test**
Yes	6(33.3%)	13(86.7%)	10(40.0%)	$\chi 2=11.06$ P=0.001***
No	12(66.7%)	2(14.3%)	15(60.0%)	

** highly significant *** very high significant

DISCUSSION

Pisa model is entirely based on the evaluation of relevant clinical symptoms and signs, and the interpretation of the electrocardiogram. Therefore, it is applicable in any clinical context

Among the symptoms, sudden-onset dyspnea is a strong predictor of pulmonary embolism. The importance of characterizing dyspnea in terms of onset has long been recognized but it was largely overlooked in most studies reported thus far Although the interpretation of the electrocardiogram requires medical expertise, the abnormalities associated with acute cor pulmonale are based on clearly defined criteria, which have been known and applied for many years

In terms of predictive accuracy, model outperformed those reported by others

Among the patients with pulmonary embolism, there was a strong relation between the clinical probability predicted by the model and higher the probability, the greater the incidence of PE.

The present model include variables that are negatively associated with pulmonary embolism. This gives the models greater flexibility, which may explain why they perform equally well in detecting and in ruling out pulmonary embolism.

Also, instead of using a point-scale score proportional to the regression coefficients, typical of other approaches we estimate the probability of

pulmonary embolism directly from the sum of the regression coefficients. This allows predicting the clinical probability as a continuous function and precise estimation of likelihood ratios.

The relative complexity of the calculation can be overcome by using dedicated software that permits online computation of clinical probability. Software is available. It can be uploaded via the Internet on desktop, laptop, and palm computers, and mobile phones.

The clinical probability predicted by the model can be used by physicians as the pretest probability in calculating the posttest probability of pulmonary embolism appropriate

The model which is found to be very useful in Italy is also very useful in India.

In Italy Model the frequencies of PE were 50% in **low** probability Geneva model,12% in low probability wells model and 5% in low probability Pisa Model

In our study the frequencies of PE were 55.6% in **low** probability Geneva model, 14% in low probability wells model and 5% in low probability Pisa Model.

In Italian Model the frequencies of PE were 39% in ***intermediate*** probability Geneva model,54 % in intermediate probability wells model and 42% in intermediate probability Pisa Model.

In our study the frequencies of PE were 40% in ***intermediate*** probability Geneva model,50 % in intermediate probability wells model and 33% in intermediate probability Pisa Model

In Italy Model the frequencies of PE were 49% in ***high*** probability Geneva model, 64 % in high probability wells model and 98% in high probability Pisa Model.

In Our Study Italy Model the frequencies of PE were 44% in ***high*** probability Geneva model, 66 % in high probability wells model and 97% in high probability Pisa Model

Our Indian study more or less follows the same results as Pisa study – Italian Model

Pisa Model is found to be better than Wells and Revised Geneva model in predicting the presence or absence of pulmonary embolism

Le Gal G, et al in a study of Prediction of pulmonary embolism in the emergency department for the revised Geneva score have found the prevalence of pulmonary embolism was 8% in the low-probability category (0 to 3 points), 28% in the intermediate-probability category (4 to 10 points), and 74% in the high-probability category (> or =11 points)

Stewart et al., in a study of the prevalence of pulmonary embolism have found 15% in the low-probability category, 29% in the intermediate-probability category, and 59% in the high-probability category

Calisir C, et al., in a study of Performance of the Wells and Revised Geneva scores for predicting pulmonary embolism have found the rates of PE in high, moderate, and low PE risk groups determined according to the Wells score and were 89.6, 26.4, 7.8 and the Revised Geneva score 83.3, 25.6, 0%, respectively.

Yap KS, et al., in a study of prospective reassessment of the utility of the Wells score in identifying pulmonary embolism have noted the likelihood of PE for a given Wells score in study was not significantly different from the likelihood in the original study by Wells et al. Scores of < 2 in our study were associated with a 4% risk of PE, scores between 2 and 6 with a 13% risk, and scores > 6 with a 67% risk.

Reshma Khetpal, MD et al., in a study of Predictability of Wells Score for the Diagnosis of Acute Pulmonary Embolism have found, among patients with positive-CTA:0%had- low probability ,62.5%had- intermediate probability and 37.5% had-high probability .Among the negative-CTA:85%had-lowprobability 15% had intermediate probability and 0% had-high probability Using high probability and intermediate probability as positve probability and low probability as negative probability for PE, the sensitivity, specificity,negative predictive value and positive predictive value were 100%,85%,100%, and 34.8%respectively

Compared with above studies Pisa Model found to be better than Wells and Revised Geneva Model

During the study we noted following

1 History of immobilisation is important

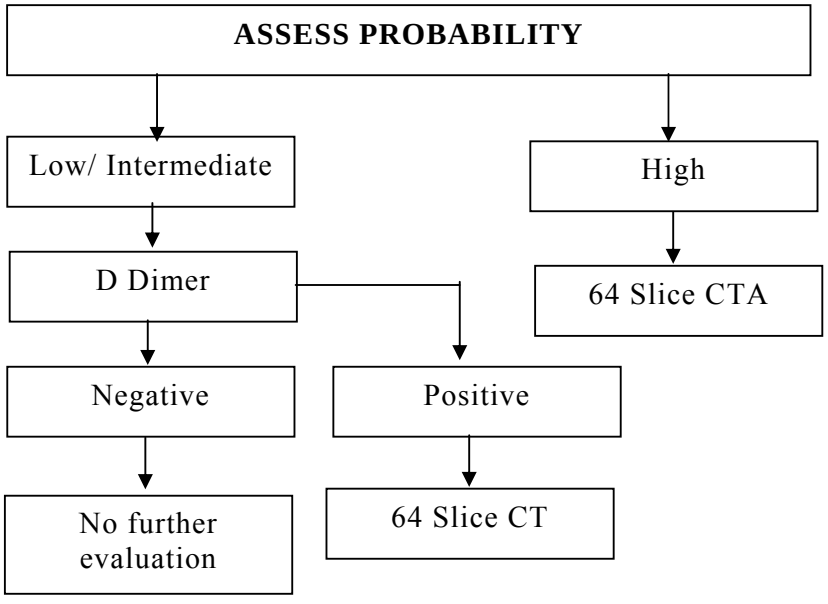
2 When ECG shows S1Q3T3or RV strain pattern one has to suspect PE in appropriate clinical setting

3 When ECHOshows RVdilataion with TR Pg 40-70mmhg with sudden onset dyspnoea, suspiscion is high

4 ECHO is ambiguous in finding thrombus in pulmonary artery because of artifact

In Emergency quick assesment of probability of PE is important because missing or not suspecting maybe fatal

USEFULNESS OF ASSESSING THE PROBABILITY



CONCLUSIONS

The diagnosis of Pulmonary Embolism primarily involves continuous vigil and probability assessment in vulnerable population.Various risk prediction models are available

1. In this study where all the three models were compared, the Italian Pisa Model is simple, easy and more accurate than other models (wells score and Revised Geneva Score) when assessing the clinical probability of pulmonary embolism in Indian population

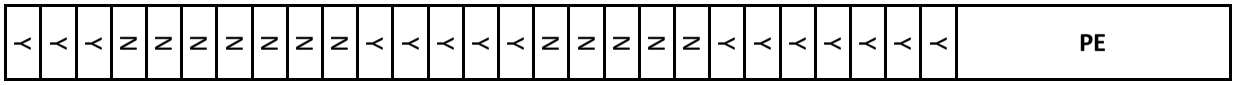
2. Predictive value of Pisa model can be further improved, if echocardiographic parameters are also incorporated in the criteria.

LIMITATIONS OF THE STUDY

1. The number of patients included in this study is less.
2. Our study population was highly selective
3. Smaller PEs may have been missed.
4. Some patients might have died before arrival to the hospital
5. IMCU patients could not be fully evaluated

S.NO	NAME	CD NO	AGE	SEX	Sudden SOB	SYNCOPE	H/O. IMMOBILIZATION	CANCER	RV Strain ECG	S1Q3T3	GENEVA	WELL	PISA	RV DILATATION	TR PG >40	DVT	D- DIMER+	64-CT PA THROMBUS
1	Janardanam	90862	54	M	Y	Y	N	N	Y	Y	I	L	L	Y	54	Y	Y	Y
2	Tamilselvi	91020	39	F	Y	N	N	N	N	N	I	L	H	N	50	Y	Y	Y
3	Kalyanasundaram	94586	50	M	Y	N	Y	Y	Y	Y	I	I	H	Y	60	Y	Y	Y
4	Fathima	100846	44	F	Y	N	Y	N	N	N	I	I	H	N	66	Y	Y	Y
5	Thulasi	105220	37	F	Y	N	Y	N	Y	Y	I	I	H	Y	48	Y	Y	Y
6	Jothi	1347	39	F	Y	N	Y	N	N	N	I	I	H	N	50	Y	Y	Y
7	Boopalan	10638	57	M	Y	N	Y	N	N	Y	I	I	H	N	52	Y	Y	Y
8	Varadarajan	89003	54	M	N	N	N	N	N	N	I	H	L	N	N	N	N	N
9	Chellammal	28242	65	F	N	N	N	N	N	N	I	H	L	N	N	N	N	N
10	Krishnamoorthy	22371	55	M	N	N	N	N	N	N	I	I	L	N	N	N	N	N
11	Seenivasan	18731	68	M	N	N	N	N	N	N	I	I	L	N	N	N	N	N
12	Sonali	1484	48	M	N	N	N	N	N	N	H	I	L	N	N	N	N	N
13	Elumalai	25500	68	M	Y	N	N	N	Y	Y	L	I	H	Y	N	N	Y	Y
14	Kanaga	26674	54	F	Y	N	N	N	Y	Y	H	H	I	Y	54	N	Y	Y
15	Anuradha	34279	67	F	N	Y	N	N	Y	N	H	H	I	N	60	N	Y	Y
16	Ravi	91663	33	M	N	Y	N	N	N	N	H	H	I	Y	70	N	Y	Y
17	Ramakrishnan	10947	26	M	N	Y	N	N	N	N	H	H	I	Y	N	N	Y	Y
18	Thirugnanam	35848	66	M	N	N	N	N	N	N	H	I	L	N	N	N	N	N
19	Chitravel	35708	65	M	N	N	N	N	N	N	H	I	L	N	N	N	N	N
20	Anthony	35508	64	M	N	N	N	N	N	N	H	I	L	N	N	N	N	N
21	Kuppusamy	1558	65	M	N	N	N	N	N	N	H	I	L	N	N	N	N	N
22	Kuppusamy	15363	62	M	N	N	N	N	N	N	H	I	L	N	N	N	N	N
23	Venkatesan	86393	30	M	N	N	N	N	N	N	I	L	I	N	N	N	N	N
24	Seenivasan	84244	38	M	N	N	N	N	N	N	I	L	I	N	N	N	N	N
25	Sarala	10780	44	F	Y	N	Y	N	Y	Y	I	I	H	Y	60	Y	Y	Y
26	Nephisa	11222	39	F	Y	N	N	N	N	N	I	I	H	N	64	Y	Y	Y
27	Nalina	11559	38	F	Y	N	N	N	Y	Y	L	I	H	Y	66	N	Y	Y

S.NO	NAME	CD NO	AGE	SEX	Sudden SOB	SYNCOPE	H/O. IMMOBILIZATION	CANCER	RV Strain ECG	S1Q3T3	GENEVA	WELL	PISA	RV DILATATION	TR PG >40	DVT	D- DIMER+	64-CT PA THROMBUS
28	Rani	12746	36	F	Y	N	N	N	N	Y	L	I	H	Y	70	N	Y	Y
29	Kumar	15101	47	M	Y	N	N	N	Y	Y	L	I	H	Y	58	N	Y	Y
30	Anand	19103	37	M	Y	N	N	N	Y	Y	L	I	H	Y	46	N	Y	Y
31	Kumar	9092	48	M	N	N	N	N	N	N	I	H	L	N	N	N	N	N
32	Sivalingam	83087	45	M	N	N	N	N	N	N	I	L	I	N	N	N	N	N
33	Prabakaran	77551	49	M	N	N	N	N	N	N	I	L	I	N	N	N	N	N
34	Nagi	169	55	M	N	N	N	N	N	N	I	L	I	N	N	N	N	N
35	Gajendran	10618	46	M	N	N	N	N	N	N	I	L	I	N	N	N	N	N
36	Selvaraj	105546	45	M	N	N	N	N	N	N	I	L	I	N	N	N	N	N
37	Dharmaraja	101787	46	M	N	N	N	N	N	N	I	L	I	N	N	N	N	N
38	Vijay	98911	20	M	N	N	N	N	N	N	I	L	I	N	N	N	N	N
39	Devasakagayam	89980	70	M	N	N	N	N	N	N	I	H	L	N	N	N	N	N
40	Arivalagan	17106	48	M	N	Y	N	N	N	N	H	H	I	N	N	N	Y	Y
41	Natarajan	63064	55	M	N	N	N	N	N	N	L	L	I	N	N	N	Y	N
42	Dhakshinamoorthy	88339	35	M	N	N	N	N	N	N	L	L	I	N	N	N	N	N
43	Damodaran	87659	57	M	N	N	N	N	N	N	L	L	I	N	N	N	N	N
44	Saroja	87046	72	F	N	N	N	N	N	N	L	L	I	N	N	N	N	N
45	Kunjithapatham	18125	68	M	N	N	N	N	N	N	H	I	L	N	N	N	N	N
46	Anbalagam	94123	42	M	N	N	N	N	N	N	H	I	L	N	N	N	N	N
47	Venkatesan	8074	55	M	N	N	N	N	N	N	H	I	L	N	N	N	N	N
48	Anwar Basha	4089	50	M	N	N	N	N	N	N	H	I	L	N	N	N	N	N
49	Raman	32114	62	M	N	N	N	N	N	N	H	I	L	N	N	N	N	N
50	Gnanasekar	31607	61	M	N	N	N	N	N	N	H	I	L	N	N	N	N	N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GLOSSARY & ACRONYMS

PE	-	Pulmonary embolism
CAD	-	Coronary artery disease
CT	-	Computed Tomography
LMWH	-	Low Molecular Weight Heparin
LV	–	Left ventricle
TTE	-	Trans Thoracic Echocardiogram.
MRI	-	Magnetic Resonance Imaging.
RV	-	Right Ventricle
EDD	–	End Diastolic Diameter
EF	–	Ejection Fraction
ECG	-	Electrocardiography
DVT	–	Deep Venous Thrombosis
RA	-	Right Atrium
RBBB-	-	Right Bundle Branch Block
ELISA-	-	Enzyme Linked Immunosorbent Assay
SHT	-	Systemic Hyper Tension
DM	-	Diabetes Mellitus
PIOPED	-	Prospective Investigation Of Pulmonary Embolism

PROFORMA

Serial no: Initials: Contact no:

Age : sex: Address:

CD no:

Diagnosis:

SHT: DM:

History of.Prolonged immobilisation

History of DVT

History of PE

History of surgery or fracture in 1 month

History of active malignancy

Unilateral limb pain

Heart rate

Pain on lower limb deep vein palpation

Sudden onset dyspnea

Chest pain

Syncope

Hemoptysis

Unilateral leg swelling

Ecg signs of acute cor pulmonale

1 T wave inversion v1 – v4

2 Tachycardia

3 S1Q3T3 pattern

4 RBBB

5 Rightaxisdeviation

Prior cardiovascular disease

Prior respiratory disease

Orthopnea

High fever

Wheeze

Crackles

Blood pressure: Pulse:

CVS: RS:

Investigations

D-Dimer

Blood sugar;

Serum creatinine:

Haemoglobin:

Complete Blood Count:

Chest X-Ray -PA view:

ECG:

ECHO parameters: 2 D, M Mode and Doppler study:

LVIDD; LVISD;

EF;

TR peak velocity;

Mcconnells sign;

Pulmonary artery thrombus;

RV dilatation;

RV function;

TDI tricuspid annulus;

PA acceleration time;

CT PULMONARY ANGIOGRAM

Thrombus